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Name:	Examiner Q. Li
Company/Firm:	U.S.P.T.O.; Group Art Unit 1632
Telecopier No.:	(703) 872-9307
Client/Matter No.:	U.S. Serial No. 09/485,421; Our Docket No. UPVG-0191
Sender's Name:	Paul K. Legaard
Pages to Follow:	13

If transmission is not complete, please call (215) 568-3100
COVER MESSAGE:

Attached is:

1) Amendment Transmittal Letter; and
2) Amendment and Request for Reconsideration.

Duplicate Submission 7/15/02

PLEASE DELIVER TO EXAMINER Q. LI IMMEDIATELY!

DOCKET NO.: UPVG-0191 **PATENT**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of: Mahalingam et al.

Serial No.: 09/485,421 **Group Art Unit:** 1632

Filing Date: October 5, 2000 **Examiner:** Q. Li

For: FUNCTIONAL FRAGMENTS OF HIV-1 VPR PROTEIN AND METHODS OF USING THE SAME

Certificate of Facsimile Transmission

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On July 9, 2002

Chad Ziegler Reg. No. 44,273

Box ☐ NON-FEE

☒ AF

Assistant Commissioner for Patents
Washington DC 20231

Sir:

REPLY TRANSMITTAL LETTER

Transmitted herewith for filing in the above-identified patent application is:

☐ A Preliminary Amendment.

☒ An Amendment Responsive to the Office Action Dated April 9, 2002.

☐ An Amendment Supplemental to the Paper filed _____.

☐ Other: _____.

sheet is provided in duplicate.

☒ The Commissioner is authorized to charge payment of the following fees and to refund any overpayment associated with this communication or during the pendency of this application to deposit account 23-3050. This sheet is provided in duplicate.

☐ The Foregoing Amount Due for Filing this Paper.

☒ Any additional filing fees required, including fees for the presentation of extra claims under 37 C.F.R. 1.16.

☒ Any additional patent application processing fees under 37 C.F.R. 1.17 or 1.20(d).

SHOULD ANY DEFICIENCIES APPEAR with respect to this application, including deficiencies in payment of fees, missing parts of the application or otherwise, the United States Patent and Trademark Office is respectfully requested to promptly notify the undersigned.

Date: July 9, 2002

Chad Ziegler
Registration No. 44,273

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DOCKET NO.: UPVG-0191

PATENT

RESPONSE UNDER 37 CFR 1.116
EXPEDITED PROCEDURE
EXAMINING GROUP NO. 1632

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Mahalingam, Ayyavoo, Patel, Kieber-Emmons, and Weiner

Serial No.: **09/485,421** Group Art Unit: **1632**

Filed: **October 5, 2000** Examiner: **Q. Li**

For: **FUNCTIONAL FRAGMENTS OF HIV-1 VPR PROTEIN AND METHODS OF USING THE SAME**

Certificate of Facsimile Transmission

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On July 9, 2002

Chad Ziegler Reg. No. 44,273

BOX AF
Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

AMENDMENT AND REQUEST FOR RECONSIDERATION

In response to the Office Action mailed April 9, 2002 in connection with the above-identified patent application, Applicant respectfully requests that the application be amended as follows.

In the Claims:

Please amend claims 1-4 and 7 to read as follows:

DOCKET NO.: UPVG-0191 **PATENT**

1. (Amended twice) A conjugated composition comprising a fragment of HIV-1 Vpr comprising amino acid sequence 17-36 and/or 59-84 conjugated to a therapeutic compound.

2. (Amended) The conjugated composition of claim 1 wherein said fragment of HIV-1 Vpr further comprises a polycationic amino acid sequence.

3. (Amended) The conjugated composition of claim 1 wherein said therapeutic compound is a DNA vaccine plasmid conjugated to said fragment of HIV-1 Vpr by ionic bonds.

4. (Amended) The conjugated composition of claim 1 wherein said fragment of HIV-1 Vpr further comprises a polycationic amino acid sequence and said therapeutic compound is a nucleic acid molecule which is conjugated to said polycationic amino acid sequence by ionic bonds.

7. (Amended) A method of delivering a compound to the nucleus of a cell comprising the step of:

contacting said cell with a conjugated compound that is either said compound conjugated to a fragment of HIV-1 Vpr protein comprising amino acids 17-36 and/or 59-84; wherein said conjugated compound is taken up by said cell and localized to the nucleus of said cell.

REMARKS

Claims 1-11 are pending in the present application. Claims 1-4 and 7 have been amended herein. No new matter has been added. Upon entry of the present amendment, claims 1-11 will remain pending.

As a preliminary matter, the attorney docket number for the present application has changed to "UPVG-0191." Applicants respectfully request that subsequent communications from the PTO bear the new attorney docket number.

I. The Claimed Inventions Are Novel

Claims 1, 3 and 5-11 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by WO9608970 (hereinafter, the "Weiner reference"). Applicants traverse the rejection and respectfully request reconsideration because the Weiner reference does not teach every feature recited in the claims.

The standard for anticipation under § 102(b) is one of strict identity. An anticipation rejection requires a showing that ***each*** limitation of a claim be found in a single reference. *Atlas Powder Co. v. E.I. DuPont de Nemours & Co.*, 224 U.S.P.Q. 409, 411 (Fed. Cir. 1984). Claims 1 and 7 each recite a fragment of HIV-1 Vpr protein "comprising amino acid sequence 17-36 and/or 59-84." Nowhere does the Weiner reference teach such a fragment of Vpr. Indeed, Applicants can only locate one portion of the Weiner reference that reports any particular fragments of Vpr protein -- page 53, lines 13-17, where fragments comprising residues 27-39, 35-48, 41-55, 49-60 and 66-68 are reported. Significantly, none of these fragments reported in the Weiner reference are the fragments comprising amino acids 17-36 and/or 59-84 recited in Applicants' claims. Thus, the Weiner reference does not anticipate Applicants' claimed invention.

The Office Action asserts that these arguments are not persuasive because claim 1 recites "comprises." Applicants respectfully disagree and submit that the Examiner cannot consider individual terms recited in a claim and interpret them in a vacuum. Claim 1 states, in part, "a fragment." Applicants teach that a fragment refers to proteins that are not complete Vpr proteins (see, for example, page 7, lines 7-13 of the specification). The position taken by the Examiner completely vitiates the explicit language recited in the claim. The term "comprising" relates to other components of the RNA that do not involve the overall number of nucleotides in the sequence. Indeed, an RNA that has forty nucleotides and the secondary structure recited in claim 87 in addition to, for example, a radiolabel would infringe claim 87. Thus, the disclosure of the entire Vpr protein sequence in the Weiner reference does not anticipate the claimed inventions.

The Office Action also asserts that because the Weiner reference reports that Vpr fragments containing "Vpr residues in a length of 3-25 amino acids" the fragments reported in the Weiner reference "**could**" comprise the fragments of Vpr recited in the claims (emphasis added). To

anticipate a claim, however, a prior art reference **must** disclose every feature of the claimed invention, either explicitly or inherently. *Glaxo v. Novopharm, Ltd.*, 334 U.S.P.Q.2d 1565 (Fed. Cir. 1995). Further, to serve as an anticipation when a reference is silent about the alleged inherent characteristic, such gap in the reference may be filled by extrinsic evidence. Such evidence, however, must make clear that the missing descriptive matter is necessarily (*i.e.*, always) present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill in the art. *In re Oelrich*, 40 U.S.P.Q. 323 (C.C.P.A. 1981); *Continental Can Co. USA Inc. v. Monsanto Co.*, 20 U.S.P.Q.2d 1746 (Fed. Cir. 1991). Inherency may not be established by probabilities or possibilities. *Id.* Further, the mere fact that a certain thing ***may*** result from a given set of circumstances ***is not*** sufficient. *Id.* Significantly, the Office Action has not established that the critical inherent characteristics are ***necessarily*** present in the Weiner reference.

Accordingly, Applicants respectfully request that the rejection under 35 U.S.C § 102(b) be withdrawn.

II. The Claimed Inventions Are Not Obvious

Claims 1-11 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over the combination of the Weiner reference and U.S. Patent No. 6,005,004 (hereinafter, the "Katz reference") or U.S. Patent No. 6,232,295 (hereinafter, the "Kayyem reference"). The Office Action mistakenly asserts that it would have been *prima facie* obvious for one skilled in the art to modify the methods of the Weiner reference by adding a polycationic peptide sequence of the Katz or Kayyem references to the Vpr conjugate composition. Applicants traverse the rejection and respectfully request reconsideration because even if the cited references are combined, the claimed invention would not be produced.

The Office Action asserts that the Weiner reference does not teach a polycationic amino acid sequence. Therefore, the Office Action attempts to cure such a deficiency by citing the Katz and Kayyem references. For the sake of brevity, the statements made above regarding the Weiner reference are incorporated herein by reference in their entirety. The Weiner reference does not teach or suggest fragments of Vpr comprising amino acids 17-36 and/or 59-84, as recited in Applicants'

claims. Neither the Katz reference nor the Kayyem reference teach fragments of Vpr comprising amino acids 17-36 and/or 59-84. Thus, the Katz and Kayyem references fail to cure the deficiency of the Weiner reference. In addition, Applicants do not agree with the conclusions drawn in the Office Action regarding the Katz and Kayyem references. In any event, the combination of the Weiner and Katz or Kayyem references fails to produce Applicants' claimed invention.

The Office Action asserts that these arguments are not persuasive because, again, claim 1 recites "comprising." As stated above, Applicants teach that a fragment refers to proteins that are not complete Vpr proteins. Again, the position taken by the Examiner completely vitiates the explicit language recited in the claim, as set forth above. Thus, the disclosure of the entire Vpr protein sequence in the Weiner reference does not anticipate the claimed inventions. In addition, that the Weiner reference reports Vpr fragments containing "Vpr residues in a length of 3-25 amino acids" does not render the claimed invention obvious. Indeed, the Office Action fails to provide any reasoning or evidence to support the position that it would have been obvious to a employ a fragment of HIV-1 Vpr that comprises amino acid sequence 17-36 and/or 59-84 or a non-HIV-1 Vpr protein that comprises amino acids amino acids 17-36 and/or 59-84, as opposed to fragments containing any other amino acid residues. The alleged motivation is, at best, an invitation for further experimentation and, at most, provides an "obvious to try" situation. However, "obvious to try" is not the standard of 35 U.S.C. §103. *In re Geiger*, 2 U.S.P.Q.2d 1276, 1278 (Fed. Cir. 1987).

Thus, in view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 103(a) be withdrawn.

III. The Claimed Invention Is Supported By Ample Written Description

Claims 1-11 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter which has not been described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants traverse the rejection and request reconsideration because Applicants' specification amply describes the claimed invention such that a person skilled in the art would recognize that Applicants had possession of the claimed invention.

The Office Action asserts that Applicants allegedly have not adequately described a conjugated composition comprising "a non-HIV-1 Vpr protein." Applicants' specification, however, amply describes the claimed inventions so as to reasonably convey to one of skill in the art that they were in possession of the claimed invention at the time of filing.

As stated in the "Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶1, 'Written Description' Requirement":

> Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, *or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention.* (footnotes omitted; emphasis added).

66 Fed. Reg. 1099, 1104 (2001). In accordance with these standards, Applicants have, indeed, provided a sufficient written description of "a non-HIV-1 Vpr protein" and a "non-Vpr protein which has a sequence of a fragment of Vpr protein."

Applicants teach, for example, at page 7, lines 14-23 of the specification that the phrase "non-Vpr protein" is meant to refer to "a protein that is not identical to HIV-1 Vpr protein." Thus, a "non-Vpr protein" is a protein that is not identical to HIV-1 Vpr protein. A *distinguishing identifying characteristic* of a "non-Vpr protein" is the fact that it is not identical to HIV-1 Vpr protein. One skilled in the art can readily determine whether any particular protein is identical to HIV-1 Vpr protein. The Office Action does not dispute this. Turning to the phrase recited in the claims -- "a non-HIV-1 Vpr protein comprising amino acids 17-36 and/or 59-84 of HIV-1 Vpr protein" -- one skilled in the art would readily understand that this refers to a protein that is not identical to HIV-1 Vpr protein but which comprises amino acids 17-36 and/or 59-84 of HIV-1 Vpr protein. Thus, the phrase "a non-HIV-1 Vpr protein comprising amino acids 17-36 and/or 59-84 of HIV-1 Vpr protein" encompasses ***any*** protein, as long as it also comprises amino acids 17-36 and/or 59-84 of HIV-1 Vpr protein. *Distinguishing identifying characteristics* of "a non-HIV-1 Vpr protein comprising amino acids 17-36 and/or 59-84 of HIV-1 Vpr protein" include the fact that it is not identical to HIV-1 Vpr

protein and that it comprises amino acids 17-36 and/or 59-84 of HIV-1 Vpr protein. Thus, one skilled in the art examining the application would understand that Applicants were in possession of proteins, which are not identical to HIV-1 Vpr, that comprise amino acids 17-36 and/or 59-84 of HIV-1 Vpr protein. Perforce, Applicants have indeed demonstrated possession by *describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention.*

In contrast to the implication in the Office Action, Applicants need not describe the detailed chemical structure of all of the encompassed molecules to demonstrate possession of a non-HIV-1 Vpr protein comprising amino acids 17-36 and/or 59-84 of HIV-1 Vpr protein. One skilled in the art would readily recognize, upon examining Applicants' specification, that ***any*** protein that is not identical to HIV-1 Vpr, but which comprises amino acids 17-36 and/or 59-84 of HIV-1 Vpr protein, is taught and, further, that Applicants were in possession of such proteins.

To advance prosecution of the present application, however, claims 1 and 7 have been amended to delete recitation of "or a non-HIV-1 Vpr protein comprising amino acids amino acids 17-36 and/or 59-84 of HIV-1 Vpr protein" without prejudice to the presentation of the non-amended claims in another application. Thus, the rejection is now moot. The claims 2-4 have been amended to be consistent with claim 1.

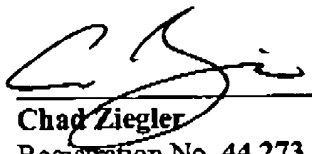
Thus, in view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph, as pertaining to written description be withdrawn.

DOCKET NO.: UPVG-0191 **PATENT**

IV. Conclusion

In view of the foregoing, Applicants respectfully submit that the claims are in condition for allowance. An early notice of the same is earnestly solicited. The Examiner is invited to contact Applicants' undersigned representative at (215) 564-8906 if there are any questions regarding Applicants' claimed invention. Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changes made.**"

Respectfully submitted,



Chad Ziegler
Registration No. **44,273**

Date: **July 9, 2002**

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DOCKET NO.: UPVG-0191 **PATENT**

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 1-4 and 7 have been amended as follows:

1. (Amended twice) A conjugated composition comprising[:]

a fragment of HIV-1 Vpr comprising amino acid sequence 17-36 and/or 59-84 [or a non-HIV-1 Vpr protein comprising amino acids amino acids 17-36 and/or 59-84 of HIV-1 Vpr protein] conjugated to a therapeutic compound.

2. (Amended) The conjugated composition of claim 1 wherein said fragment of HIV-1 Vpr [or said non-HIV-1 Vpr protein] further comprises a polycationic amino acid sequence.

3. (Amended) The conjugated composition of claim 1 wherein said therapeutic compound is a DNA vaccine plasmid conjugated to said fragment of HIV-1 Vpr [or said non-HIV-1 Vpr protein] by ionic bonds.

4. (Amended) The conjugated composition of claim 1 wherein said fragment of HIV-1 Vpr [or said non-HIV-1 Vpr protein] further comprises a polycationic amino acid sequence and said therapeutic compound is a nucleic acid molecule which is conjugated to said polycationic amino acid sequence by ionic bonds.

7. (Amended) A method of delivering a compound to the nucleus of a cell comprising the step of:

contacting said cell with a conjugated compound that is either said compound conjugated to a fragment of HIV-1 Vpr protein comprising amino acids 17-36 and/or 59-84 [or said compound conjugated to a non-HIV-1 Vpr protein comprising amino acids 17-36 and/or 59-84 of HIV-1 Vpr protein]; wherein said conjugated compound is taken up by said cell and localized to the nucleus of said cell.

☐ Applicant(s) has previously claimed small entity status under 37 CFR §1.27.

☐ Applicant(s) by its/their undersigned attorney, claims small entity status under 37 CFR §1.27 as:

- ☐ an Independent Inventor
- ☐ a Small Business Concern
- ☐ a Nonprofit Organization

☐ This application is no longer entitled to small entity status. It is requested that this be noted in the files of the Patent and Trademark Office.

☐ Substitute Pages _____ of the Specification are enclosed.

☐ An Abstract is enclosed.

☐ _____ Sheets of Proposed Corrected Drawings are enclosed.

☐ A Certified Copy of each of the following applications: _____ _____ is enclosed.

☐ An Associate Power of Attorney is enclosed.

☐ Information Disclosure Statement.

- ☐ Attached Form 1449.
- ☐ A copy of each reference as listed on the attached Form PTO-1449 is enclosed herewith.

☐ Appended Material as follows: _____.

☐ Other Material as follows: _____.

FEE CALCULATION

☒ No Additional Fee is Due.

	REMAINING AFTER AMENDMENT	HIGHEST PAID FOR	EXTRA	SMALL ENTITY RATE	SMALL ENTITY FEE	NOT SMALL ENTITY RATE	NOT SMALL ENTITY FEE
TOTAL CLAIMS	11	27 (20 MINIMUM)	0	$9 EACH	$0	$18 EACH	$
INDEP. CLAIMS	2	9 (3 MINIMUM)	0	$42 EACH	$0	$84 EACH	$
FIRST PRESENTATION OF MULTIPLE DEPENDENT				$140	$0	$280	$
☐ ONE MONTH EXTENSION OF TIME				$55	$0	$110	$
☐ TWO MONTH EXTENSION OF TIME				$200	$0	$400	$
☐ THREE MONTH EXTENSION OF TIME				$460	$0	$920	$
☐ FOUR MONTH EXTENSION OF TIME				$720	$0	$1440	$
☐ FIVE MONTH EXTENSION OF TIME				$980	$0	$1960	$
☐ LESS ANY EXTENSION FEE ALREADY PAID				minus	($ 0)	minus	($)
☐ TERMINAL DISCLAIMER				$55	$0	$110	$
☐ OTHER FEE OR SURCHARGE AS FOLLOWS:					0		
TOTAL FEE DUE					0		$

☐ A Check is Enclosed in the Foregoing Amount Due.

☐ Petition is hereby made under 37 C.F.R. 1.136(a) to extend the time for response to the Office Action of @@ to and through @@ comprising an extension of the shortened statutory period of @@ month(s).

☒ The Commissioner is hereby requested to grant an extension of time for the appropriate length of time, should one be necessary, in connection with this filing or any future filing submitted to the U.S. Patent and Trademark Office in the above-identified application during the pendency of this application. The Commissioner is further authorized to charge any fees related to any such extension of time to deposit account 23-3050. This